

Kentucky Lung Cancer Research Program

Fiscal Year 2009 Annual Report

University of Kentucky

Lucille Parker Markey Cancer Center

for

Kentucky Health Care Improvement Authority

And

The KLCR Program Governance Board

Council for Postsecondary Education

August 11, 2009

August 12, 2009

Kentucky Health Care Improvement Authority

Tobacco Settlement Funding Report

Kentucky Lung Cancer Research Program
University of Kentucky
Annual Report
FY 2009

1. Please summarize any progress or achievement toward the goals of your program that have been met during this reporting period.

The Kentucky Lung Cancer Research Program at the University of Kentucky/Markey Cancer Center has five primary components:

- A. An Administrative component
- B. A component targeted toward attainment of National Cancer Institute Designation
- C. The Kentucky Clinical Trials Network
- D. A Core Program/Project Support component
- E. An Investigator-Initiated project component

Progress in these areas is summarized as follows:

A. Administration

This component, substantially reduced in scope from previous activity with the loss of the Executive Director position, nonetheless continued to assure progress in the functions of all institutional components of the program.

B. National Cancer Institute Designation

Progress toward this premier benchmark goal was evident of several fronts:

1. Brought the search for a new Center Director to a successful conclusion with the recruitment of B. Mark Evers, M.D. from the University of Texas Medical Branch at Galveston. Dr. Evers is a nationally recognized Surgeon, former Director of the UTMB Comprehensive Cancer Center and Director of the Sealy Center for Cancer Cell Biology. He brings a major SPORE grant in colorectal cancer, as well as numerous other independent and collaborative grants in aging, organ development and cancer. In addition to serving as Director of the Markey Cancer Center and Professor and Vice Chair for Research in the Department of Surgery, Dr. Evers serves as Physician-in-Chief of UK Healthcare Cancer Services and holds the Markey Cancer Foundation Endowed Chair.

2. Recruited 10 new research scientist faculty, all part of a new team working with Dr. Evers, with total NIH and American Cancer Society funding of more than \$13 million.
3. Continued scientific productivity of basic and clinical scientists in receipt of new grants and contracts and publication of research results (detailed updates to follow);
4. Continued encouragement of collaborative activity by designated Program Leaders;
5. Advanced the Core KLCR and Markey Program/Project Support components (see individual core component updates below);

C. Kentucky Clinical Trials Network

The Kentucky Clinical Trials Network (KCTN) fulfills a legislative mandate through the Kentucky Lung Cancer Research Program to *“establish a statewide clinical trial network to make university-based clinical trials available to the community physician in order to bring the most innovative cancer treatments to all Kentuckians in need of these treatments.”*

The KCTN functions as an engaged alliance of regional, local and university hospitals in partnership with community physicians for the execution of promising clinical trials throughout the Commonwealth. The network agenda is guided by the interests and expertise of multiple specialty healthcare professionals, including: pulmonologists, medical oncologists, radiologists, and surgeons.

The Network leadership team for this continually developing program facilitates identification and development of collaborative projects across disciplines, supported by the operational infrastructure of the KCTN Coordinating Center.

Two notable changes were made in the operational infrastructure during 2009. First was a move of the KCTN headquarter offices to a new service base at the following address:

2317 Alumni Park Plaza, Suite 100
Lexington, KY 40517
1-800-671-4077

This location provides much more amenable conferencing and program expansion space with easy access immediately off New Circle Road in Lexington.

The second change was the addition of a new position for an Administrative Research Assistant. This position provides critical support for expanded central operations in data capture using specialized data systems, as well as liaison with remote participating sites and documenting, monitoring and publishing site activities. This includes maintenance of routinely updated website content.

Milestones for FY 2009:

- KCTN Coordinating Center Team conducted 70+ Site Visits during FY2009; regular Interim Site Visits, special Education Site Visits, specific Study Support Site Visits and Study Initiation Visits.
- 10 prospective new sites are in various stages of development.
- Continued development of Quality Assurance Core in collaboration with regionally based clinical investigation resource to evaluate and improve process for current clinical data monitoring for all KCTN sponsored studies.
- Representatives from 6 Site IRBs participated in the Regional IRB Consortium Workshop. “Representatives from 2 Site IRB's and KCTN Coordinating Center participated in Planning Committee for 3rd IRB Consortium Workshop, “Improving Human Subjects Protection through Collaboration”.
- Representatives from 5 Site's and their IRBs participated in the conference “Human Subjects Protection: Still Challenging After All These Years” .
- Representatives from 5 Sites participated in continuing education in research conduct Workshop “Research 201, Junior & Senior Years”.
- KCTN members & Coordinating Center participated in annual symposium hosted by University of Kentucky, Markey Cancer Center, Multidisciplinary Lung Cancer Program, “Lung Cancer Symposium: Evolving Strategies in Lung Cancer Diagnosis and Treatment”
- Initiated and maintained communications and development support to 7 prospective members.
- Continued project planning and development for investigator-initiated projects.
- Expanded patient population served by KCTN sites and enrolled to KCTN studies to 52/120 counties; 43% of state.
- Total patients accrued to KCTN studies now exceeds 140.
- CTN-0501 Data Monitoring Committee, December meeting, evaluated current study findings, safety, and study progress. Recommended without delay study continuation thru interim analysis, as request by Coordinating Center.
- CTN-0505 Completed Study Accrual with statistically significant findings of immune response to investigational product vaccine.
- Continued development of study design for next phase of 1650G vaccine investigation. Project Planning Team comprised of representatives from 5 sites participated in study design and protocol development. Project pending protocol approval at IRBs and study drug manufacture.

Study Pipeline--Open Trials:

Treatment Study: *CTN-0501, Chemotherapy with or without Dexamethasone. Examining reduction in blood toxicities and increased effectiveness of anti-tumor effects of chemotherapy*

Patient Population: Untreated Stage IIIB/IV, NSCLC

Investigator-Initiated Project: John Rinehart, MD Study Chair

Study Plan: 9 Sites conducting study

Project Funding: KCTN & Eli Lilly

Subjects Accrued = 59

Treatment Study: *CTN-0602, Comparator of 2 Chemotherapy Regimens, Examining effectiveness of combination therapies and Quality of Life*

Patient Population: Extensive Stage Small Cell Lung Cancer

Industry-Sponsored Project: Eli Lilly, International Trial

Study Plan: 8 Sites Participated

Project Funding: Eli Lilly

Subjects Accrued = 7

Treatment Study: CTN-0505, Allogenic Cellular Vaccine 1650-G

Examining immunologic response to vaccine measured by number of T cells that react to specific antigenic stimulus

Patient Population: Stage I/II Lung Cancer

Investigator-Initiated Project: Edward Hirschowitz, MD & John Yannelli, PhD

Study Plan: 4 Sites

Project Funding: KCTN & UK Commonwealth Collaborative

Study to date results have generated concept for next phase examination of vaccine; study in development noted below.

Subjects Accrued = 12

Epidemiology Study: CTN-0601, Examining Lung Cancer Survival: Smoking Cessation, Quality of Life, Environmental Exposures

Patient Population: Early Stage Lung Cancer, post surgery

Investigator-Initiated Study: Claudia Hopenhayn, PhD

Study Plan: Conduct at up to 10 sites for total of 200 subjects

Project Funding: KCLRP Cycle 7 & KCTN

Subjects Accrued =43

Observational Study: Examine Impact of Ethnic Origin by Observation of Clinical Outcomes of Patients Treated per Routine Clinical Care with Alimta

Patient Population: Stage IIIB/IV, 2nd line therapy, NSCLC

Industry-Sponsored Study: Eli Lilly

Study Plan: 1 Site participating

Project Funding: Industry, \$52,900 (20 subjects)

Subjects Accrued =1

Treatment Study: PR104-2003:A Randomized Phase II, Multi-Center, Open-Label Trial of PR104 and Docetaxel in Patients with Advanced Non-Small Cell Lung Cancer

Patient Population: Stage IIIB/IV

Industry-Sponsored Study: Proacta

Study Plan: 1 Site participating

Project Funding: Industry \$109,570 (5 subjects)

Subjects Accrued = 0

Treatment Study: Efficacy of ZD 6474(Zactima) Versus Placebo after Prior Therapy with EGFR TKI (Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor)

Patient Population: Stage IIIB/IV

Industry-Sponsored Study: AstraZeneca

Study Plan: 2 Sites participating

Project Funding: Industry

Subjects Accrued= 2

Study Pipeline--Regulatory Start-Up

Treatment Study: Randomized Trial of Pemetrexed Plus/Minus Allogeneic Cellular Vaccine 1650-G as Maintenance Therapy For Nonsquamous Non-Small Cell Lung Cancer (NSCLC)

Patient Population: Stage IIIB/IV, Second-Line

Investigator-Initiated Project: Edward Hirschowitz, MD, John Yannelli, PhD & CTN-0804 Project Planning Team

Study Plan: In development, feasibility and FDA communications ongoing. Projected Start Spring 2009

Project Funding: In negotiation; KCTN

Specimen-Collection Study: *Prospective Collection of Biospecimens; specimens banked and available to researchers examining lung cancer issues*

Patient Population: All Lung Cancers

Investigator-Initiated Project: Joseph Pulliam, MD & Mike Cibull, MD

Study Plan: Pilot at local hospital to ensure integrity of specimens; expand regionally

Project Funding: KCLRP & KCTN

Treatment Study: CP02-0452: Randomized Phase III Study of Docetaxel or Pemetrexed with or without Cetuximab in Patients with Recurrent or Progressive Non-Small Cell Lung Cancer after Platinum-Based Therapy

Patient Population: Stage IIIB/IV, Second-Line

Industry-Sponsored Study: ImClone

Study Plan: Conduct in up to 5 sites for up to 50 subjects total

Project Funding: Industry, budget in negotiation

Prevention Study: Lung Cancer Patient Statement to Smoker Family Member with Participation in Cooper Clayton Smoking Cessation Program

Patient Population: Smokers Family Members of Lung Cancer Patients

Investigator-Initiated Project: Catherine Martin, MD & Project Planning Team

Study Plan: In development, Grant submitted to agencies for funding consideration.

Project Funding: Pending grant announcements

Epidemiology Study: Cultural Beliefs on Biospecimen Collection & Use

Patient Population: Lung Cancer Patients & General Population

Investigator-Initiated Project: Project Planning Team Working

Study Plan: In development, study design and NIH grant submission pending

Project Funding: Pending

KCTN Study Sites (19):

University of Kentucky

University of Louisville

Lexington

Louisville

Owensboro Medical Health System	Owensboro
Western Kentucky Hematology & Oncology Group	Paducah
Commonwealth Cancer Center	Danville
Commonwealth Cancer Center	Richmond
Commonwealth Cancer Center	Frankfort
Commonwealth Cancer Center	Somerset
Commonwealth Cancer Center	London
Commonwealth Cancer Center	Corbin
Montgomery Cancer Center	Mt. Sterling
Our Lady of Bellefonte Hospital	Ashland
St. Claire Regional Medical Center	Morehead
King's Daughters Medical Center	Ashland
Kentucky Cancer Center	Hazard
Lexington Clinic	Lexington
St. Joseph HealthCare	Lexington
Central Baptist Hospital	Lexington
Lake Cumberland Regional Hospital	Somerset

D. Core Program/Project Support

1. "Marty Driesler Lethal Cancers Project"

In 2004, this Fifth Congressional District project was initiated in Southeastern Kentucky under an authorization from the Centers for Disease Control. A primary component of the project was to identify early biomarkers of lung cancer in high-risk individuals, based on both repetitive CT scans and analysis of biospecimens from serum, exhaled respiratory condensate, and urine. Risk level was defined by age, smoking history and compromised lung function. This study became a close companion study to KLCR Early Detection initiatives. As Phase I funding expired on CDC support, the lung component of the project was subsumed by KLCR. Targeted accrual of over 500 subjects (with 249 having completed first phase processing) has been attained to date. Follow-up processing and testing continues through 2013. SPECIAL NOTE: While the purpose of this early detection study is to identify markers and abnormalities that may be signs of early lung cancer, the study has given rise to numerous incidental findings. CT scans identified 120 additional findings, including coronary artery calcification, emphysema, and abnormalities in the airway, skeleton, and diaphragm areas. The results of these tests were forwarded to the participants' physicians for medical decision-making and follow-up. UK Project Staff continue to evaluate medical records of all participants in order to assess the efficacy of this study.

2. In support of multiple KLCR projects and an expanding translational research enterprise, the Markey Cancer Center established and continues development of a Biospecimen Core Program (BCP) to collect, document, preserve and distribute human-derived biological samples for authorized investigations. The BCP is a critical resource for a. clinical correlative studies to help decipher molecular signatures of tumors associated with poor prognostic outcome; b. to help identify biomarkers for early diagnosis or for therapeutic targeting; and c. to help predict and/or monitor tumor

response to treatment. The BCP was initiated through KLCR funding and continues to serve as a critical reference resource for both current and future lung cancer studies

Subject specific data has been transitioned from the BCP database into an official caTissue database. The latter conforms to National Cancer Institute standards for certifiable Biospecimen Core operations. The BCP now enters new data for new specimens directly into caTissue in real time. Efforts are ongoing to determine if additional data can be annotated from other databases to create robust information, that will allow researchers to search for specific types of biospecimens to enhance their research efforts. The following table shows the number of specimens that are stores at the BCP (with corresponding information stored in caTissue). Since the last report, xxx new tissue has been acquired by BCP.

Study	No. of Participants	No. of Samples In BCP Storage
BUK 040447 Lung	341	6593
Drielser 040714 Lung	252	12,317
SPN 020171 Lung	63	732
Versatile 040454 Lung	436	4535
Versatile 040454 head/Neck	55	289
Ovarian Screening 050129 Ovarian	845	5910
Total	1992	30,376

E. Investigator-Initiated Projects

A summary of the Cycle 9 grant solicitation is given below. Applications are currently in the process of peer-review, which should be completed by early September.

<http://kentuckylungcancer.org/>

- **Announcement Release Date:** March 18, 2009
- **Letter of Intent Date:** April 17, 2009

- **Application Due Date:** June 15, 2009
- **Applications Received:** 12
- **Awards:** Pending

2. Please indicate any challenges that were encountered during this reporting period related to the program's goals and objectives, administration or other project factors.

A. The loss of former Project Director, Bonnie Sigafus, in June 2008 continued to be felt throughout FY 2009. However, the cooperative engagement and patience of all constituencies has been most helpful in keeping the multiple components of the project moving forward.

B. Accommodation of the expanding budget for the Kentucky Clinical Trials Network became a significant challenge, with a budget increase to a level of \$970,000 in FY2009. This expansion occurred in the face of a diminishing allocation of KLCR funds (Note 2.C.1-3, below). The UK/UL budget distribution differential of 58/42 originally established to fund KTCN activity amounted to \$497,776 in FY2009, leaving a differential of \$472,224 to be derived from other programmatic elements. A budget of \$1,183,318 requested for KCTN in FY2010 is under current evaluation. UK and UL leadership are committed to the success of this component of the KLCR program and will be reviewing overall KLCR Program obligations to determine how best to fulfill the combined legislative mandates.

C. It has been found that an increasing apportionment of funds is being taken "off the top" from Kentucky Lung Cancer Research Program to support Ovarian Cancer Screening. Initially allocated \$775,000 annually per year, the OCS apportionment increased to \$975,000 in FY2009. This funding now exceeds that of any KLCR program element except for KCTN and the combined institutional allocations for investigator-initiated grants.

D. The availability of space, particularly state of the art research space, has been a recurring challenge in program expansion, particularly hampering the recruitment of new faculty. However, this concern is being addressed with new research facilities scheduled to come on-line in the new 278,000 sf Biological Pharmaceutical Complex Building by the end of 2010. The Markey Cancer Center will have access to approximately 20,000 sf of new space in this new building. The proximity to faculty and scientists in the College of Pharmacy will further solidify collaborative activities in Experimental Therapeutics.

3. Please provide a report on the expenditure of tobacco settlement funds during this reporting period.

A Financial Report is provided on page 10, following:

Financial Report for 4th Quarter, FY 2009
University of Kentucky

Programmatic Initiative	Funds Available as of 03/30/09	Previous Expenses as of 03/31/09	Expenses 4 th Quarter	Encumbered Expenses	Funds Available FY2008-2009
Kentucky CTN	675,366	200,248	198,416	0	276,702
Early Detection					
Marty Driesler Project	245,264	16,947	33,600	27,584	167,133
Solitary Pulmonary Nodule	0	0			0
UK-Twin for OLBH	52,631	30,283	8,864	289	13,195
Biospecimen Core Program	295,369	73,937	68,843	0	152,589
Informatics Connection	5,628	0	0		5,628
NCI Designation (1)	498,634	10,659	10,797	0	477,178
External Grants Review	34,425	300	0	0	34,125
Epidemiology	0	0	0		0
Administration	254,307	37,717	37,223	0	179,367
Pilot projects	45,997	18,326	7,041	0	20,630
Prime & closed accounts	1,991	0	0	0	1,991
Total/Net (2)	2,109,613	388,417	364,783	27,873	1,328,540

Footnotes:

1. Earmarked \$442,516 in NCI Designation Funds to fund additional grants.
2. Received residual distribution of \$528,420 included in above numbers.
3. Received new programmatic funds for 2009 allocation \$1,804,400
PADR's still pending amount not show in above totals.

4. Please indicate if your program has met the requirement to hold a public hearing on the expenditure of funds during this reporting period. If so, please include documentation regarding the hearing (for example, notices publicizing the hearing, handouts, minutes, media coverage, etc.) Please indicate any comments received, positive or negative, on the proposed use of funds.

A public meeting of the Kentucky Lung Cancer Research Program Governance Board was held on February 12, 2009. Minutes of that meeting are appended. No public comments were received.

Current Members

Kentucky Lung Cancer Research Program Governance Board

Name	Representing
Eaton, John W., PhD	UofL
Flanagan, Dan	CPE
Means, Robert T., MD	UK
Miller, Donald M. . MD, PhD	UofL
Mullett, Timothy W., MD	UK
Paris, Kristie J., MD	State-at-Large
Roach, James P., MD	State-at-Large
Roberts, Bonnie	State-at-Large
Turner, John S.	CPE

Kentucky Lung Cancer Program Governance Board

Meeting Minutes

February 12, 2009

Kentucky Council on Postsecondary Education

Frankfort, KY

Attendees: Kristie Paris (Chair), Dan Flanagan (CPE), Donald Miller (UofL), John Eaton (UofL), Lewis Kelly (Proxy for Robert Means/UK), Tim Mullett (UK), James Roach (SAL), Bonnie Roberts (SAL), Guests: Chad Bowman, Beth Yost, Jason Green, Milton Pierce, Diane Konzen, Linda Linville.

The Governance Board of the Kentucky Lung Cancer Research Program was brought to order by Chair, Dr. Kristie Paris, with introduction of new board members and guests.

Discussion followed regarding the KLCRP's Strategic Plan and the legislative requirements to conduct revisions and report those to the Council and Health Care Improvement Authority (HCIA). Dr. Sigafus had begun this process in the spring of 2008, but it was not completed during the last biennium (06-08). Current documents are being researched to determine next steps with an action item for Drs. Miller and Kelly to bring a proposal to the April Governance Board meeting.

With regard to a strategic plan, discussion pursued regarding the need for an Executive Director position to be filled to track the program's budget, accomplishments, Clinical Trial Network and other initiatives funded by the Tobacco Settlement awards made to the institutions. With 10 years of funding, the halfway mark has been reached. Having appropriate accountability and tracking were identified as essential to best utilize capacity of funding. It was suggested that perhaps current staff could manage the program although there was no disclaimer from the staff, but rather administrative determination. With further investigation, this issue will be analyzed and the duties/responsibilities of each institution with regard to the directorship of the program determined, including an evaluation of the need for a director, tasks required, et al.

During the November 2008 Governance Board meeting, Cycle 8 Investigator-Initiated (I-I) grants were recommended totaling \$1,942,559. The balance of the I-I Grants Reserve Funding for 07-08 is \$1,675,011.50. With the addition of the 08-10 I-I Grants Reserve Funding, the balance of these funds through FY 2010 is \$4,675,011.50. With a carry-forward balance and \$3M in reserve for the 08-10 years, the group discussion lead to the need for a report from investigators regarding findings, career positions, other end-points, accountability measures for the investment in I-I researchers. Such accountability should be included in a 10-year report as well as annual reporting to the Council. It was suggested to conduct a survey of all KCLRP grantees to determine the impact of their research efforts.

The amount of funding that the KLCRP has received in the last 10 years and with 10 years of Tobacco Settlement funding remaining, the board discussed the need to have an external audit of the program conducted. With consensus for such review, the Board felt confident that other states' with similar work conducted with Tobacco Settlement funds could assist with a thorough evaluation and perhaps lend

consultation to Kentucky's investment and 10 year plan for the remaining years of the program. It was felt that an evaluation also would be meaningful to legislators and the HCIA. After reviewing Kentucky's Report Card produced by the American Lung Association related to lung cancer, and the state's failing grades, much work remains for changing behaviors of tobacco users through prevention, screening, and effective treatment for lung cancer. Kelly, Miller, and Mullett felt they had clinical contacts that could be pursued to find appropriate reviewers. An idea to have a panel discussion at a Kentucky-sponsored Lung Cancer Summit was discussed as a venue fitting for shared evaluative information. A tentative summit date in the month of November was considered with Diane Konzen drafted to spearhead a draft agenda. A three-pronged Summit to include education, research, and clinical best practices was considered with possible inclusion of a student-research proposal competition. Setting the stage for the next 10 years, where Kentucky wishes to be in regard to research and reduction in lung cancer morbidity and mortality will be topics of discussion in the coming months and as a Summit is planned.

The Board was reminded of their need to file annual reports with the Council and, although quarterly reports have been due the HCIA, during the November 2008 meeting a representative from the Authority proposed annual reporting to them consistent with Council reporting. Consistency with what and how to report was encouraged by the Authority and the Council's Audit Report from 2008.

Dr. Roach entertained discussion on research he has been conducting on Vitamin D deficiency and its possible relationship to lung cancer and other health-related illnesses. He suggested supporting Vitamin D deficiency screening for all women. He, along with others also supported the Governance Board's support of legislation to increase the cigarette excise tax proposed in recent days. Flanagan suggested a press release from the Board and a letter of support for the higher increase in this tax as proposed by Governor Beshear. Dr. Mullett drafted a letter of support for immediate submission.ⁱ

The Board determined that their work was important and that bi-monthly meetings would be important setting a date for April 15, 2-4 PM in Frankfort at the Council offices.

Paris challenged the Board to be active in translation of research findings by the KLCRP to community practice and reminded all of any related public policy based on bench marked studies.

Mullett advised the Board of the need to report on current activities of the Clinical Trials Network. His concern that community physicians have not been numerous relates to the expanse of work needed for patients to participate. A full report of the KCTN will be provided at the April 2009 meeting.

Next meeting date set for April 15ⁱⁱ.

Meeting adjourned at 4:15 PM.

ⁱ With legislative committees in session, a news release from the Board was prepared and released to the media (2/12/2009, with letters of support to key legislators electronically sent on 2/13/2009).

ⁱⁱ As of 2/24/09, meeting date changed to April 22 to accommodate those planning on attending national conference week of April 15.